THE ETIOLOGY OF ZYMOTIC ENTERITIS

(EPIDEMIC DIARRHŒA)

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BY

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PREFACE

In the course of the last ten years the author has been engaged in an investigation of the conditions of disease as found in infants. Seven years ago he had provisionally determined the essential causes of the disease—*zymotic enteritis*; but he was not prepared to offer any precisely formulated explanation of the relationship existing between the organisms responsible for the disease and the processes by which the disease attacked the infant. He had, however, arrived at the conclusion that it was not an infectious disease, and that, if it were due to a specific organism, then the action of that organism was governed by rules widely divergent from those usually governing the action of specific pathogenic bacteria.

Three years later he conceived the explanation which is advanced in these pages. But he was unwilling to publish statements so diametrically opposed to current opinion and practice until he had tested them by check and counter-check. The results of his later and latest investigations may be inferred from the fact that his conclusions are now published.

Desiring to lay these conclusions before the members of his profession, the author in November, 1909, submitted an article embodying an account of the etiology of the disease, as here presented, to one of the leading medical journals. After submission of the proof, the Editor decided that it would be unwise to publish it unless it were modified to meet his opinions. The author does not desire to lay any stress upon this, except in so far as it explains the present publication.

The somewhat detached nature of the account is due to the fact that it will form part of the fourteenth chapter of the third edition of the 'Nutrition of the Infant.'

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ZYMOTIC ENTERITIS is the most fatal disease of infancy, and, despite the advances which sanitation has made in this country, no corresponding improvement is observable in the infant mortality rates. On the contrary, it has been clearly shown by Newman that Epidemic Diarrhœa (the official name of the disease) is steadily increasing as a factor in the causation of death among infants under one year of age. He contrasted the death-rates of infancy in the years 1845-1849 with the rates for the years 1899-1903, the figures being derived from the Registrar-General's reports for the two periods. These figures show that the deaths arising from epidemic diarrhœa and from conditions of immaturity at birth have greatly increased:

'Diarrhœa, which formerly caused the death of 10 per cent. of dead infants, has increased in half a century to 15 per cent.; respiratory diseases have risen from 16 to 18 per cent.; and prematurity from 17 to 29 per cent. . . . Other children's diseases are vanishing or have vanished. There has been a vast improvement in the general environment surrounding their lives, but the problem of infantile mortality still remains because of the *increase* in these diseases — prematurity, pneumonia, and diarrhœa.'[1]

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[1] 'Infant Mortality,' pp. 55, 56.

The group of conditions broadly indicated by the terms immaturity, prematurity, or congenital defect, are of great importance, for they show that antenatal conditions are responsible for a large proportion of deaths occurring in infancy. These deaths are sharply distinguished from those arising from causes that affect the infant after birth by the fact that the deaths arising from congenital defect occur for the most part in the first few weeks of life, and practically all of them within the first three months.

The great increase in the proportion of deaths caused by 'epidemic diarrhœa' cannot, however, be so accounted for. The disease may attack the infant at any age, but its greatest intensity of attack is not exercised upon the youngest infants, but upon infants between the ages of four and eight months.

The increase in the proportion of deaths from respiratory diseases is probably closely connected with the increase in diarrhœa.

Healthy infants are not very frequently attacked by serious disease of the lung as a primary affection. In a certain number of quite young infants a sub-acute bronchitis may be observed. It is very chronic in character, and it is generally stated to have been present at birth or soon afterwards. This is the common type of bronchitis in infants who are born the victims of congenital syphilis.

In conditions of enteritis, pneumonia is extremely likely to develop as a complication. It occasionally occurs in the acute disease, but it is commonly seen accompanying the more chronic conditions. It is a freqnent accompaniment or sequela of atrophic enteritis, and many infants suffering from this disease contract pneumonia as a terminal affection.

With regard to zymotic enteritis, it is necessary to lay stress upon the fact that the disease is an extremely acute one and is widely removed in its clinical characters from the chronic digestive derangements from which infants commonly suffer as the result of improper feeding.

The necessity for insisting upon this discrimination is shown by the confusion which exists amongst various writers, and which is well illustrated in a series of cases recently published. Some of the cases appear, from the account, to be clearly cases of zymotic enteritis; others are almost equally clearly not instances of this disease. Indeed, one infant is described as weighing 14½ pounds at five months of age, and as having suffered from epidemic diarrhœa *since birth.*

The infants most liable to suffer from the disease in its most violent and fatal form are those in whom alimentary disorders have been established for some time. Their condition is one in which the processes of zymotic enteritis find their unfettered opportunity. In some cases it may be difficult to establish the line of demarcation between the simple and the toxic enteritis: nevertheless, the clinical types are essentially distinct. The disease is so fatal that the consideration of its etiology and of the methods by which it may be prevented is of much greater moment than that of the precise therapeutic measures to be adopted when the infant is attacked. For, with the most expert treatment available, the recovery of the infant is in reality dependent upon the dose of poison the infant has received, the precise degree of virulence of the poison, and the constitutional vigour of the infant.

It therefore becomes necessary to examine the evidence available as to the causation of the disease. Elaborate researches have been carried out by various authorities, with the result that the following facts are clearly established:

The disease is most prevalent and most fatal during the third quarter of the year. The higher the temperature of the late summer, the greater the prevalence of the disease, especially if this high temperature be associated with but little rain. In other words, meteorological conditions involving a high temperature with much dust are those which promote the conditions which accompany the greatest incidence of the disease. Other authorities—notably, Dr. J. T. C. Nash, of Norwich, and Dr. Niven, of Manchester—have drawn attention to the part played by flies in the dissemination of the disease.

The classical researches of Ballard,[1] the more recent researches of Newsholme,[2] and the observations made by many Medical Officers of Health, all establish clearly that the essential factors are high temperature and dust, with special reference to the part they play in the contamination of milk. Three of Newsholme's conclusions are of particular importance:

1. Epidemic diarrhœa is chiefly a disease of urban life.
2. Epidemic diarrhœa as a fatal disease is a disease of the artisan and still more of the lower labouring classes to a preponderant extent This is probably largely a question of social status *per se;* that is, it is due to neglect of infants, uncleanly storage of food, industrial occupation of mothers, etc.
3. The fundamental condition favouring epidemic diarrhœa is an unclean soil, the particulate poison from which infests the air and is swallowed, most commonly with food, especially milk.

These facts thus ably elucidated by these observers are incontrovertible, and it becomes necessary to carry our inquiry a step farther, and elucidate, if possible, the precise character of the poison which is responsible for the disease, and the manner in which it is conveyed to the infant.

In the first place, it is essential to the comprehension of the disease that the common conception that it belongs to the group of specific infectious diseases should be abandoned. Zymotic enteritis is in no sense of the word an infectious disease, and it cannot be conveyed by contagion.

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[1] Supplement to the Report of the Medical Officer of the Local Government Board, 1887.

[2] Public Health, 1899-1900.

The work of the Infants Hospital is confined exclusively to infants under twelve months of age. All the infants when admitted are seriously ill, most of them desperately so. At the times that zymotic enteritis is prevalent very numerous cases are admitted, mostly of an extremely severe type. Since the establishment of the hospital over 1,000 in-patients have been treated. No infant has ever contracted the disease in the hospital. The only infants suffering from zymotic enteritis are those suffering from the disease at the time of admission. No attempt at isolation is made. The infants lie side by side in their cots—the case of severe atrophy next the case of zymotic enteritis—and they are all tended by the same nurses, who minister to all their requirements.

Precisely the same thing is seen outside the hospital. At a time that the disease is sweeping through a town, destroying some hundreds of infants per thousand in the course of a month or two, there are babies living in the most insanitary conditions who are immune. They are the breast-fed babies. There is no need to labour this point, for numerous Medical Officers of Health have drawn attention to the same fact.

Between the circumstances of the poor Irish breast-fed baby living in a London slum and those of the infant warded in the Infants Hospital there is a wide contrast. There is also a remarkable correspondence. Both are fed on a pure *raw* milk. The infants at the hospital are protected by something much more powerful than isolation, for it is a practical impossibility for the violent fatal disease known as zymotic enteritis to occur in an infant fed on fresh milk. It is essential for the development of the disease that the characteristic properties of the natural food of the infant should have been destroyed by heat, by preservatives, or by some other means.

The proper care of milk implies that it shall be handled in such a manner that the development of all organisms in the milk is prevented, whether they be beneficent or otherwise. But even when milk is not guarded so carefully as this, it is protected by its peculiar qualities from decomposition in the ordinary sense of the word. Milk left to itself at ordinary temperatures undergoes a chemical decomposition peculiar to itself. The lactose is converted into lactic acid by means of the lactic acid bacillus, and when the production of the acid has reached a certain point the caseinogen of the milk is coagulated, the action of the acid being exactly the same as regards the precipitation of the curd as that of any other acid—acetic, hydrochloric, etc.

In the case of infants fed on milk that has undergone this lactic decomposition, digestive disturbance is extremely likely to occur and diarrhœa is almost certain to ensue. But the affection is altogether different from the conditions seen in zymotic enteritis. (1) The diarrhœa is 'simple'—*i.e.*, it is due to an excess of a constituent normally present in the alimentary canal; (2) appropriately treated, the infant will soon recover; (3) there is a complete absence of the *toxæmia* which is the characteristic and fatal feature of zymotic enteritis.

Such conditions, however, ought to be prevented, and the fact that milk is not in a fit condition for consumption can be readily detected, owing to the characteristic smell of lactic acid, even when this has only been formed in very small amount, so small that it is insufficient to curdle the milk. When the milk has not been cooked there is therefore a natural danger-signal, indicating that it is not sufficiently fresh.

The fundamental character of this reaction is that it entirely prevents any changes occurring in milk of a poisonous character. Moreover, the production of lactic acid is by no means unlimited. When the amount of acid produced has reached a certain point (considerably less than 1 per cent.),[1] the lactic bacilli are inhibited, and thus a condition is reached in which no further development of lactic organisms can occur, while no other organisms can develop, since these require an alkaline or neutral medium.

The organisms which are responsible for the production of zymotic enteritis are universally distributed. They exist in the mouth of every healthy infant. They are the ordinary organisms of putrefaction, but they cannot attack milk in its natural state.

For the incidence of zymotic enteritis certain general conditions must obtain:

1. The milk must be boiled (pasteurized or sterilized), or so treated by heat, or by preservatives, or by some other means, that the lactic organisms are either destroyed, or their action inhibited.

2. The milk must then be subjected to conditions which allow of a development and culture of the putrefactive organisms.

Since the condition of the milk with regard to the lactic organisms is the essential point, the other means by which their action may be prevented require to be mentioned. When the milk mixture prepared for an infant is made from raw milk, the mixture may comply to a greater or less extent with the specified conditions in certain circumstances. In the preparation of the food of the young infant, cow's milk is considerably diluted, equal parts of milk and barley-water, supplemented by a little cane sugar, being a common mixture. If this mixture is made in bulk from boiled milk, and is allowed to stand for some considerable time, the danger in hot and dusty weather is extreme. But even when made from raw milk the danger is always present, for the growth of the lactic organism depends upon the presence of lactose; in the diluted mixture the amount of lactose is much reduced, and consequently the production of lactic acid is much diminished; while the barley-water and the cane-sugar directly favour the organisms dangerous to the infant. Apart from the above treatment, nearly all methods commonly employed in the domestic preparation of the infant's food favour the development of putrefactive organisms. The addition of an alkali, such as lime-water, hinders the protective action of the lactic bacilli, for the alkali neutralizes the acid to a greater or less degree. Other factors not directly concerned with the handling of the milk prior to administration predispose to the disease. Many infants suffer seriously from chronic indigestion, in consequence of the mass of casein which their gastric and intestinal secretions have to deal with. Even in such a commonly used mixture as equal parts of milk and water, the casein is present in a proportion about three times as great as in the food received by the healthy infant when breast-fed. As a result of this excess, the normal fermentations are greatly hindered. The bacilli common to the large intestine become more and more established in the small intestine. The intestinal dejections in consequence give evidence of putrefactive changes. These are pre-eminently the conditions predisposing to the incidence of the disease.

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[1] The following experiment was carried out by Revis and Payne:

Two litres of milk obtained under very careful conditions were inoculated immediately after milking with a coagulated milk culture of *B. acidi lactici*. The milk was kept at 65° to 67° F.

The percentage of lactic acid formed (in grammes per 100 c.c.) was as follows: 24 hours, 0·0230; 48 hours, 0·0710; 72 hours, 0·1285; 96 hours, 0·2725; 116 hours, 0·3570.

Diluted condensed milk of the ordinary variety is probably the agent responsible for the disease in its most fatal and devastating form. Here, every condition has been fulfilled that the putrefactive organisms may acquire their fullest activity. The condensed milk when diluted contains so minute an amount of lactose as to render it a negligible quantity. The lactic organisms have been entirely destroyed, and putrefactive changes are the only changes that can occur.

Boiled milk is, however, the type of the food commonly used and fulfilling the conditions for the development of the disease, and it is necessary to consider the actual resultant processes as they affect the infant belonging to the mother of the poorer classes.

Owing to certain physical peculiarities of milk, it is practically an impossibility for the mother to raise milk to a temperature of 212° F. At about 190° F. it 'scalds' or boils over, and it is at about this temperature that the milk is removed from the fire. No more effectual means could be devised to promote the development of the conditions responsible for the incidence of zymotic enteritis. The boiling effectually destroys the lactic organisms, but it makes no impression on the spores of the putrefying bacteria. Much higher temperatures and much longer exposure are required to kill these. It is the condition of the milk *after* the boiling that constitutes the critical and imminent danger to the infant. Even if the mother carefully employs the only method of cooling at all available to her, she has to reduce the temperature of a fluid at about 190° F. by means of running water, which as it comes from the tap, in the summer, is at a temperature of about 70° F. This latter temperature is nearly the *optimum* temperature for the putrefactive organisms, so that their prolific and luxuriant growth inevitably ensues. In the process of transferring the milk from the saucepan to a jug or other vessel in which the milk is to be kept occurs the first contamination after boiling. The mother may cover the milk with a saucer or by some other domestic means, but it is practically certain that dust will find its way to the milk, when the circumstances of the poor home are considered. Moreover, the frequent intervals of feeding render the liability to contamination extreme. Within two or three hours the milk will again be thoroughly exposed, in order that the next feed may be prepared, and thus the increase of putrefactive bacteria and their poisonous products proceeds throughout the day.

The simple fact is, that if a bacteriologist were asked to state the measures necessary to convert a safe milk into one which was a virulent poison, he could not greatly or essentially improve upon the method as carried out by the mothers of the poorer classes at a time when the temperature is 80° F. in the shade, and dust and flies are everywhere.

It cannot, however, be too strongly emphasized that these organisms of putrefaction do not directly produce the disease. Even when myriads of them reach the alimentary canal of the infant, as they do in contaminated boiled milk, they are still quite unable directly to attack the infant. They are unable to live in the tissues of the living body. Their action is one which is exercised entirely upon the milk, either inside or outside the infant.

The changes they produce in milk are the changes directly connected with their essential function as putrefactive organisms. They act upon the albuminoids as albuminoid-dissolvers, and create, by their action upon these constituents, virulent chemical poisons. It is these chemical poisons which develop under the conditions that have been described, which produce the toxæmia characteristic of zymotic enteritis, and which are so virulent that they destroy the infant in the course of a few days by their poisonous action upon the cellular tissue throughout the body.

The effective cause of zymotic enteritis is not the organisms which finally promote its production, but the methods by means of which the infant has been deprived of its natural safeguards against them.

The fundamental characteristic of the natural food of the infant is that it is a raw fluid. In all circumstances the cooking of milk for the use of infants gravely impairs its nutritive value. With regard to zymotic enteritis, no serious amelioration in the mortality arising from this disease can be anticipated until the fullest protection of pure raw milk is secured for every infant, and special precautions must be taken, at times when heat and dust are prevalent, to secure that the milk for the use of infants shall be preserved fresh and unboiled.

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